1. Weight loss as a treatment imperative for the obese psoriasis patient


Summary
The role of weight loss as part of the treatment paradigm for psoriasis patients has not been evaluated prospectively. This is despite the accumulating evidence that the mechanisms underpinning obesity-induced inflammation may contribute to the systemic inflammation that manifests in psoriasis. Consequently, the authors embarked on a prospective randomized trial involving 60 overweight patients with psoriasis and two dietary regimens. Half of the patients were randomized to a low-energy diet (LED) for 16 weeks. For the initial 8-week period, patients followed the Cambridge Diet, limiting caloric intake to 800–1,000 kcal/day, with food consisting mostly of meal bars, shakes, soups and porridge. For the second 8 weeks, their caloric intake was increased to 1,200 kcal/day by incorporating regular meals. The control group followed a conventional diet according to the Danish guidelines for a healthy all-around diet. Interestingly, patients were allowed to maintain their anti-psoriatic therapies (including methotrexate and biologic treatments) if they had been stable and unchanged for the prior 3 months. The mean Psoriasis Area and Severity Index (PASI, primary endpoint) and Dermatology Life Quality Index (DLQI, secondary endpoint) scores after 16 weeks were both reduced by 2.0 points on the respective scales. The comparative PASI endpoint showed a trend toward a decrease, with a P value of 0.06, and the DLQI was statistically significant with a P value of 0.02.

Cont., Page 3
A LETTER FROM THE PRESIDENT

It is my distinct honour, as the International Psoriasis Council’s (IPC) new board president, to welcome you to the July 2014 issue of IPC’s Psoriasis Review. I am proud to have the opportunity to lead this organization and build on the impressive gains made under the strong leadership of my predecessor, Professor Peter van de Kerkhof, during his three-year tenure.

I want to express my own thanks and the gratitude of all IPC councillors to Professor van de Kerkhof for his dedication, as board president, to making IPC a leading organization in research, education and management of psoriasis and its comorbidities. I am grateful that he will continue to lend his advice and expertise as a member of the IPC board.

As you may know, I was among the founders of IPC in 2004 and I am pleased to see how far we have come in the past decade. We have made great strides in our goal to become a global psoriasis leader. In a Q&A feature on page 24 of this issue, I outline my vision and goals for IPC as we move forward.

In addition to the Q&A, you will find in this issue our regular “Top 5” feature – reviews of the top five clinical and research articles nominated and chosen earlier this year by IPC councillors. For this issue, the articles had to be published either in print or electronically between July 1 and Dec. 31, 2013.

Also in this issue:

- Writer/dermatologist Dario Kivelevitch reports on discussions about psoriasis that took place at the 72nd Annual Meeting of the American Academy of Dermatology (AAD) in March.

- You’ll meet IPC’s new CEO Steve O’Dell.

- IPC Councilor Dr. Claudia de la Cruz reports on the 32nd RADLA conference that took place in Santiago, Chile, in May.

- We have launched “The Shifting Paradigm in Psoriasis Treatment,” a series of CME meetings designed to provide healthcare providers with the latest information on psoriasis comorbidities and treatment options.

- We have formed an exciting partnership with the International Federation of Psoriasis Associations (IFPA) and the International League of Dermatological Societies (ILDS) to develop a Global Psoriasis Atlas. Its goal is to expand our understanding of the relevance and burden of psoriasis.

- Four new councilors have joined our ranks.

I want to acknowledge and thank the co-editors of this issue, Dr. Linda Stein Gold of the Henry Ford Health System in Detroit, Michigan, and Dr. Michel Gilliet of the Central Laboratory of Hematology at the University of Lausanne, Switzerland.

We hope you’ll find this issue both interesting and informative. I look forward to working with all of you to continue to advance our knowledge of the disease and better care for patients with psoriasis.

For additional copies of IPC’s Psoriasis Review or to learn more about IPC, visit www.psoriasiscouncil.org.

With best wishes,

Professor Chris Griffiths, MD, FRCP, FMedSci
President, International Psoriasis Council
Manchester, United Kingdom
Cont. from page 1

Concomitantly, the mean body weight loss was 15.5 Kg, (P<0.01) in the LED group versus controls. Thus, weight loss in a psoriasis patient displayed an impact on the clinical appearance of the condition as well as the patient’s quality of life. Consequently, obese patients with psoriasis should be encouraged to lose weight to dampen the systemic inflammation that contributes to the skin condition as well as to ameliorate the potential for undesirable cardiovascular comorbid outcomes.

**COMMENTARY** This study is important because it showed a trend toward an effect of weight loss on psoriasis severity despite the small number of patients and relatively small baseline PASI values. One can speculate that the effect is due to a diminished cytokine load from fat tissue, resulting in reduced systemic inflammation in the body leading to amelioration of psoriasis symptoms. Regardless, this study should encourage dermatologists to incorporate dietary programs into treatment regimens for moderate to severe psoriasis, particularly for those patients who are obese. This study and its results expand on those previously reported from an IPC-sponsored clinical trial, which showed a trend toward a decrease (Paller et al, Association of Pediatric Psoriasis Severity with Excess and Central Adiposity: An International Cross-Sectional Study. JAMA Dermatol. 2013;149(2):166-76). The trial investigated the relationship between excess adiposity and the severity of the psoriasis. In this trial, the odds ratio (95% CI) of obesity (body mass index ≥95th percentile) in children with psoriasis vs controls was 4.29 and was higher with severe (4.92) than with mild (3.60) psoriasis. In addition, Jensen, Zachariae et al have subsequently, extended the observations to study the effect of weight loss on the cardiovascular risk profile of obese patients with psoriasis (Acta Derm Venereol. 2014 February 20. [Epub ahead of print]). In this later analysis, weight loss was correlated with significant reductions of diastolic blood pressure, resting heart rate, total cholesterol, VLDL cholesterol, triglyceride, plasma glucose, glycated haemoglobin, and tissue plasminogen activator inhibitor. This study augmented the contention that both the psoriasis condition and cardiovascular risk profile of obese patients can be significantly improved by successful weight-reduction programs.

For additional copies of IPC’s Psoriasis Review or to learn more about IPC, please visit www.psoriasiscouncil.org.
2. Targeting IL-12P40 ameliorates both psoriatic skin and joint symptoms


Summary
Given the comorbid association of psoriatic arthritis in 20–30% of patients with psoriasis, it is an important finding that ustekinumab, an anti-IL-12p40 monoclonal antibody previously approved for the treatment of moderate to severe psoriasis, also has a positive impact on joints. The multicenter, phase 3 trial conducted in sites across Europe, North America, and Asia consisted of 615 adult patients with active psoriatic arthritis randomly assigned to standard 45-mg ustekinumab, 90-mg ustekinumab, or placebo at weeks 0, 4, and every 12 weeks thereafter. Crossover to ustekinumab occurred at week 16 and thereafter in patients not exhibiting a minimal response to therapy. The results demonstrated a statistically significant (P<0.0001) positive impact of ustekinumab on psoriatic arthritis as measured by the proportion of patients who achieved 20 percent improvement, according to American College of Rheumatology criteria. On safety, there were no reported events of opportunistic infections (including tuberculosis), death, or malignancies by week 52. However, episodes of cholecystitis were noted in two patients, salpingitis in one patient, erysipelas in one patient, and a pharyngolaryngeal abscess in one patient. In addition, no major adverse cardiovascular events occurred in any treatment group by week 16. However, one serious cardiac adverse event (angina pectoris) was reported during the placebo-controlled period in a patient given placebo, a non-fatal stroke in one patient and two myocardial infarctions post week 16. These results confirm and extend the prior observations of the impact of ustekinumab on psoriatic arthritis. Moreover, the results contribute to the understanding of the pathogenesis of psoriatic skin and joint disease by affirming that the targeting of IL12p40 and/or the cytokines IL-12 or IL-23 provides a viable therapeutic regimen.
3. Targeted exome sequencing validates alleles associated with psoriasis, but reveals limited knowledge of overall genetic risk for psoriasis


Summary
The evolution of gene sequencing technology increasingly permits large-scale genome analysis efforts. Tang and colleagues have capitalized on these advances to perform a comparative sequence analysis of the coding regions (ie, exomes) from 781 psoriasis patients and 676 controls. The goal was to identify common and rare mutations that result in an amino acid change, leading to a functional impact on the exome-derived protein (ie, nonsynonymous mutation). This systematic approach revealed 1,326 genes that contained single nucleotide variants (SNVs) between the two groups. The relevance of the SNVs in the candidate genes selected were validated by the targeted sequencing of these specific regions in 9,946 psoriasis cases and 9,906 controls from the Chinese Han population. In total, more than 80,000 nonsynonymous SNVs were identified within these genetic regions, of which the majority (>97%) were rare. However, 6 common and low-frequency nonsynonymous SNVs displayed a consistent association with psoriasis contained within the genes’ encoding: IL-23R (IL-23 receptor), GJB2 (Gap junction beta-2 protein), LCE3D (late cornified envelope 3D), FUT2 (Galactoside 2-alpha-L-fucosyltransferase 2), and ERAP1 (endoplasmic reticulum aminopeptidase 1). Each of these regions has been previously identified as being associated with psoriasis and, thus, the results herein confirm the evidence of association. Additionally, the association with psoriasis of other previously reported nonsynonymous SNVs was validated (eg, CARD14, TARBP1 and ZNF816A). However, single-variant and gene-based association analyses of nonsynonymous SNVs did not identify any newly associated genes for psoriasis in the regions subjected to targeted resequencing. This suggests that coding variants in the 1,326 targeted genes contribute only a limited fraction of the overall genetic risk for psoriasis.

COMMENTARY
Genetic technology advances have permitted the sequencing of the entire coding and noncoding human genome. The findings illustrate that there are approximately 20,000 protein-coding genes that account for less than 2% of the total genome. The rest is associated with non-coding RNA molecules, regulatory DNA sequences, or intron sequences yet to be assigned any role or function, but which may indeed have an impact on human disease. While we are some distance away from being able to perform full genome sequence analysis for individual patients compared to controls in a statistically meaningful manner, today’s methodologies only permit the large-scale sequencing of targeted exomes or coding regions within subjects. In this study, Tang et al have leveraged the latest methods in an attempt to identify and confirm the association of various gene mutations with psoriasis. Such mutations have been previously identified in genome-wide association studies that are based upon the prior identification of allelic variability and, thus, are limited with regard to detecting new associations. The data support and extend the prior knowledge of the genetic alleles associated with psoriasis, yet also reveal that there is more work to do to define the susceptibility to psoriasis. This is because the nonsynonymous SNVs in the 1,326 targeted genes were found to have limited contribution to the overall genetic risk of psoriasis. As well, the authors acknowledge the limited potential of the approach to detect very rare SNVs, even those with strong effect. Consequently, the complete picture of the genetic susceptibility to psoriasis and other human conditions awaits further advances in genetic technology that will facilitate statistically meaningful, large-scale, full genome sequencing in patients and controls.
4. Identification of a pharmacogenetic marker of response to biologic therapy in psoriasis


Summary

A widespread association of a variety of genetic alleles with psoriasis has been illustrated by genome-wide association scans (GWAS) and targeted exome sequence strategies, such as that presented by Tang and colleagues, as reviewed on page 5. More limited is a connection between genetics and the response to therapies that might portend stratified treatment paradigms in the future. In this study, Talamonti and associates performed a retrospective, case-controlled study of the impact of various gene polymorphisms known to be associated with psoriasis susceptibility on the response to treatment with ustekinumab. Moderate to severe psoriasis patients (51 total, 37 males and 14 females) were treated with ustekinumab according to the product label wherein patients received doses of 45 mg (if less than 100 Kg) or 90 mg (if more than 100 Kg) at weeks 0, 4 and every 12 weeks thereafter. Genotyping was performed on genomic DNA isolated from the venous blood of each patient, using allele-specific primers in a standard polymerase chain reaction. The results indicated that 55% of the patients (28) were HLA-Cw6 positive and 45% HLA-Cw6 negative (23). The frequency of the LCE3B/3C gene deletion occurred in 65% of patients and TNFAIP3 in 34%. Genes LCE3B/3C and TNFAIP3 encode products that are downstream of IL-23 in the pathogenic cascade of psoriasis. While the LCE3B/3C and TNFAIP3 polymorphisms were found to not correlate with response to ustekinumab, the HLA-Cw6 allele was found to be associated with a faster and higher clinical response rate. At week 12, statistically higher numbers of HLA-Cw6-positive patients (96%) achieved PASI 75 versus only 65% of HLA-Cw6-negative patients. In addition, the response rate was faster with 89% of HLA-Cw6POS patients reaching PASI 50 by week 4, compared to only 61% HLA-Cw6NEG patients. The responses remained significantly different through the 40-week study period. Thus, HLA-Cw6 not only contributes to psoriasis susceptibility, but also to the patients’ response to therapy.

COMMENTARY

On the journey toward customized treatment regimens for individual patients, there is a need for pharmacogenetic markers of response to predict efficacy, safety, toxicity and long-term tolerability of the agents within the available armamentarium. HLA-Cw6 seems to fulfill the criteria for this need as it relates to ustekinumab therapy, thus opening up the possibility of genetically-dictated treatment paradigms for the patient with psoriasis. The results demonstrate a remarkable and significant difference in the response to ustekinumab that likely should be evaluated in larger prospective controlled studies. Of interest is whether the results indicate differences in the clinical form of psoriasis manifest according to HLA-Cw6 positivity. Or is the result a consequence of the biological function of the HLA-Cw6 gene product as it relates to IL-12 or IL-23, the cytokine target of the ustekinumab monoclonal antibody? In this regard, it is interesting to speculate that psoriasis-propagating antigens are presented in the context of HLA-Cw6 to a subset of IL-17 secreting cytotoxic CD8+T cells that are abundant in psoriasis epidermis and activated in the presence of IL-23. Also of interest is whether the HLA-Cw6 association with ustekinumab is shared across other therapy classes. Previous reports have indicated that response to the TNF class of biologics is higher in HLA-Cw6-negative patients and might be preferentially associated with the TNFAIP3 gene. Thus, the capacity to customize a patient’s treatment regimen based upon pharmacogenomics might be a step closer, based upon this “proof of principle” study that predicts response to biologic therapy in psoriasis.
5. Genetic differentiation indicates multiple forms of generalized pustular psoriasis with distinct etiology


Summary
Researchers have made great progress in defining the genetic basis for a subset of familial generalized pustular psoriasis (GPP), which was found to be associated with mutations in the interleukin-36 receptor antagonist (IL-36RN) gene. GPP can present in patients with or without psoriasis vulgaris (PV) suggesting that there may be two forms of GPP that are etiologically distinct. In this study by Sugiura et al, the objective was to map the prevalence of IL-36RN mutations in 31 Japanese GPP patients in order to better define the etiology of GPP. Direct sequencing analysis of exons and intron–exon boundaries of IL-36RN revealed that 9 out of 11 GPP-alone patients had homozygous or compound heterozygous IL-36RN mutations. In contrast, only two siblings out of 20 cases of GPP with PV displayed compound heterozygous mutations in IL-36RN. Quantitative reverse-transcriptase polymerase chain reaction was used to determine that the mutation resulted in the expression of truncated mRNA encoding IL-36RN. HLA typing was performed on the two siblings carrying the IL-36RN mutations and their healthy brother. The results revealed that the two GPP-afflicted siblings also carried the HLA-A*0206 haplotype that is known to be associated with susceptibility to PV. Immunohistochemical staining of skin specimens revealed almost no expression of the IL-36RN protein in patients with GPP alone, compared to strong expression in the granular layers of the epidermis in patients with GPP plus PV who had no IL-36RN mutation. Thus, the authors propose that GPP alone is a distinct subtype of GPP relative to GPP with PV that is genetically programmed due to the homozygous or compound heterozygous mutation of IL-36RN.

COMMENTARY The genetic basis of GPP has been the subject of much scientific progress in the past few years. In the June 2012 issue of IPC’s Psoriasis Review, we reviewed the paper from Marrakchi et al (“Interleukin-36-Receptor Antagonist Deficiency and Generalized Pustular Psoriasis”), which reported a homozygous missense mutation in nine Tunisian families. Subsequently, in the December 2013 issue, we reported on the initial work by Sugiura and colleagues, which demonstrated that mutations in the IL-36RA-encoding gene (IL-36RN) are characteristic for only a subtype of Japanese GPP patients. The current report represents the extension of this initial observation by Sugiura et al, which delivers compelling evidence that GPP alone is a distinct subtype of GPP caused by mutation in the IL-36RN gene and which is etiologically distinct from the GPP that appears with PV. This evolving understanding of the root cause of disease portends new therapeutic strategies to combat GPP alone, as well as for the GPP associated with PV.
Experts address pathophysiology, management of psoriasis during annual meeting

By Dario Kivelevitch, MD

Dario Kivelevitch is a dermatologist from Buenos Aires, Argentina, currently completing a 2-year translational research fellowship focusing mostly on psoriasis at Baylor Institute for Immunology Research, Dallas. He will be starting his residency training in dermatology in July 2015 at Baylor University Medical Center under the supervision of Dr. Alan Menter. He has also completed an internal medicine residency and received his doctor of medicine degree from the University of Buenos Aires. Earlier this year, Kivelevitch received a one-year, $40,000 National Psoriasis Foundation fellowship grant to study the blood and skin of people with palmo plantar pustular psoriasis to try and understand how it develops.

Psoriasis pathophysiology and management were prevalent topics at the March 2014 American Academy of Dermatology (AAD) annual meeting in Denver, Colorado. National and international psoriasis experts presented new findings and results of new clinical trials. Following are summaries of these discussions.

Immunopathogenesis
IPC Councilor Dr. Frank Nestle of St. John’s Institute of Dermatology, King’s College, London, presented an overview of the latest advances in the immunopathogenesis of psoriasis. Over the past decade, researchers have been gaining in their knowledge of the intricate network of events underlying psoriasis pathogenesis. Recent studies have exposed the key role of the interleukin 23/T helper (Th17) cytokine axis in psoriasis. Th17 cells are characterized in part by their production of IL-17. Activated dermal dendritic cells produce, among other cytokines, IL-23, which in turn promotes the expansion of the Th17 population, thus sustaining the Th17-cell-dependent chronic inflammation in psoriasis. There is a novel subset of immune cells that have shown to be a potent source of IL-17. This new subpopulation is called innate lymphoid cells (ILCs). ILCs are a group of cells with lymphoid morphology which lack antigen-specific receptors such as those expressed by T and B cells. Therefore, they do not respond in an Ag-specific manner. ILCs are effector cells that release cytokines to exert their function. Based on their cytokine production profile and surface markers, three groups have been defined: ILC1 (producing Th1 cytokines), ILC2 (producing Th2 cytokines), and ILC3 (producing Th17 cytokines). Group 3 ILCs (ILC3) are characterized by the transcription factor RORγt, respond to IL-1β and IL-23, and produce IL-17 and/or IL-22. Data from numerous studies indicate that ILCs are key sources of IL-17 and IL-22 production in epithelial inflammatory disease such as Crohn’s disease. Furthermore, the ILC3 group has been found to be present in higher numbers in psoriatic skin compared to healthy skin. Nevertheless the exact role of this cellular population in psoriasis remains to be elucidated.

Clinical management
Topical therapy
IPC Councilor Dr. Mark Lebwohl, dermatology department chair, Mount Sinai School of Medicine, New York City, discussed new agents in the pipeline for topical therapy, the most commonly used form of psoriasis treatment. “Yet advances in topical treatments have not kept up with major advances made in systemic therapy.” Topical steroids and vitamin D derivatives remain first-line treatments. Recently, researchers have conducted clinical trials testing new formulations and vehicles. New topical agents in different stages of development were discussed during this session. They included JAK, MEK1, STAT and PDE4 inhibitors, pan-selectin antagonists and new nonsteroidal anti-inflammatories. Results of a topical tofacitinib trial were presented.

Topical tofacitinib was evaluated for efficacy in a phase 2a randomized, double blind, vehicle-controlled trial. Seventy-one patients were randomized to 2% tofacitinib or placebo for twice-daily application to a target plaque area for 4 weeks. The primary endpoint of percentage change from baseline in target plaque severity score (TPSS) at week 4 revealed a significant difference for the tofacitinib group. No severe adverse events (SAEs) were reported.
The number of patients who reported burning or stinging at the treatment site was small and occurred with similar frequency across all groups.4

**Phototherapy**

This session – presented by Drs. John Y. M. Koo, Department of Dermatology, University of California, San Francisco; Henry W. Lim, Department of Dermatology, Henry Ford Hospital, Detroit; and Giovanni Leone, San Gallicano Dermatologic Institute (IRCCS), Rome, Italy – reviewed the state of the art of phototherapy.

One of the most effective psoriasis treatments available, phototherapy is a first-line option for many patients living with the disease. Narrowband UVB (NBUVB) is more effective than broadband UVB and safer than PUVA (ultraviolet light A combined with psoralen). Phototherapy use is recommended due to its favorable benefit/risk ratio, low cost compared to other systemic treatments, and widespread availability.

Reasons to avoid the use of phototherapy include increased risk of carcinogenesis, photoaging, short-term side effects such as skin irritation and burning, and inconvenience for the patient. Phototherapy is indicated for different clinical forms of psoriasis, such as plaque psoriasis or palmo-plantar psoriasis with soak PUVA (soaking affected areas in a solution of water that contains psoralen before exposure to UVA).

Phototherapy is not indicated for erythrodermic and pustular psoriasis and, with the exception of targeted therapy, is not usually indicated for difficult areas such as scalp and skin folds.

The efficacy of phototherapy has been studied in several trials. In one study, PASI 75 was achieved at week 12 by 55% of patients treated with NBUVB,5 88% of patients treated with PUVA,6 100% of patients treated with PUVA plus retinoids,7 and 100% of patients treated with Goeckerman therapy.8

The major risk in phototherapy is the increased possibility of skin cancer associated with its use. In a 2005 review of the literature, authors Lee, Koo and Berger found no increased incidence of skin cancer associated with UVB phototherapy.9 Two studies10,11 found an increased risk of nonmelanoma skin cancer associated with the use of PUVA in Caucasian subjects. Another two studies couldn't find a higher incidence of melanoma in patients treated with PUVA.11,12

A small study to assess the risk of cutaneous cancer and PUVA bath therapy was not able to find an increased incidence of any skin cancer associated with this treatment.13 Data in the literature regarding the carcinogenic effect of NBUVB are not conclusive. Animal studies demonstrate a carcinogenic effect, whereas retrospective studies in humans have not demonstrated an increase in skin cancer incidence, possibly due to intrinsic study limitations. Although phototherapy is cost-effective, one downside is its inconvenience for the patient. UVB and PUVA treatments require 30 to 40 sessions to achieve a marked improvement.

One of the most effective psoriasis treatments available, phototherapy is a first-line option for many patients living with the disease. Phototherapy use is recommended due to its favorable benefit/risk ratio, low cost compared to other systemic treatments, and widespread availability.

Targeted therapy seems to overcome this limitation. According to one recent report, it is possible to achieve PASI 75 in 2 to 4 sessions using sub-blistering dosimetry with an 308-nm excimer laser to treat a generalized psoriasis patient.14 The same group published similar clinical results of an ongoing, open-label pilot study in which they used targeted phototherapy with a 308-nm excimer laser combined with clobetasol spray and calcitriol ointment to treat moderate to severe generalized psoriasis.15 Preliminary results showed that 76% of patients achieved PASI 75 by week 12.
Assessment of the optimal treatment dose is done by measuring the minimal blistering dose (MBD) in contrast with the minimal erythema dose (MED) traditionally used in phototherapy.

There is also a prolonged remission with laser treatment, with up to 80% of the patients remaining at PASI 50 6 months after treatment was discontinued. One advantage of targeted phototherapy is that it is not limited by tolerance of non-involved skin. It can clear psoriatic plaques in as few as 2 to 4 treatments. With the most powerful laser, it can treat up to 20% body surface area in 15 to 20 minutes. Because UVB exposure is limited to involved skin and has a long remission period, it may decrease cumulative UVB exposure.

Systemic therapy
Classic systemics
Dr. Lebwohl reviewed the classic systemic treatments, focusing particular attention on toxicity and adverse events (AEs). Since its approval by the U.S. Food and Drug Administration (FDA) in 1972, methotrexate (MTX) has become the most used systemic agent for the treatment of moderate to severe psoriasis. Safety and monitoring of MTX has been an ongoing concern. MTX has shown to have an acceptable efficacy in psoriasis, achieving a PASI 75 in 40% of patients at 12 to 16 weeks. Hepatotoxicity is a well-known adverse effect associated with MTX. Early diagnosis and prevention of hepatotoxicity and hepatic cirrhosis have been significant challenges, as clear evidence toward management of these adverse effects is still missing.

Previously, guidelines for the use of MTX recommended a baseline biopsy, plus routine liver biopsy with cumulative doses.

Methotrexate was FDA-approved for rheumatoid arthritis in 1998. In contrast to dermatology guidelines, the American College of Rheumatology did not recommend liver biopsies on patients receiving MTX. The 1998 consensus on using MTX to treat psoriasis16 introduced a change: Experts removed the need for a baseline biopsy and recommended a liver biopsy at 1-1.5g in patients with no history or evidence of liver disease. Finally, in 2009, guidelines for the management of psoriasis17 recommended changes in managing liver biopsies. The guidelines do not recommend baseline biopsy; rather, they recommend considering liver biopsy after 3.5-4.0g total cumulative dosage in patients with no underlying risk for hepatotoxicity or liver disease, along with monitoring. The guidelines present further information on monitoring and a different algorithm for the management of patients with increased risk of liver disease.17

...methotrexate (MTX) has become the most used systemic agent for the treatment of moderate to severe psoriasis. Safety and monitoring of MTX has been an ongoing concern... Early diagnosis and prevention of hepatotoxicity and hepatic cirrhosis have been significant challenges, as clear evidence toward management of these adverse effects still is missing.

The risk of developing liver fibrosis or cirrhosis was assessed in a 1982 study that evaluated liver biopsies after treatment with MTX. It found that after 5 years of treatment, 24% of patients had developed liver fibrosis or cirrhosis.18 Liver biopsies are an invasive procedure with an associated risk for the patient. A retrospective 21-year study evaluating 9,212 liver biopsies showed that the rates of death and major hemorrhage after a liver biopsy were 0.11% and 0.24%, respectively.19

Based on the risk associated with liver biopsies, it is suggested that those patients with increased risk for developing liver fibrosis should undergo this procedure, while for patients with minimum risks, liver biopsies may not be indicated or the frequency may be markedly reduced.20 Risk factors for developing hepatic toxicity from methotrexate should be carefully assessed in all patients prior to starting MTX therapy. These risk factors include: a history of or current excessive alcohol consumption; persistent abnormal liver chemistry studies; history of liver disease, including chronic hepatitis B or C; family history of
inheritable liver disease; diabetes mellitus; obesity; history of significant exposure to hepatotoxic drugs or chemicals; lack of folate supplementation; and hyperlipidemia.

When monitoring patients on MTX treatment, it is relevant to keep in mind that increased liver function tests (LFTs) are not related to the development of liver fibrosis.\textsuperscript{21} The addition of folic acid to the MTX regime can prevent an increase in LFTs\textsuperscript{22} and gastrointestinal symptoms such as nausea.\textsuperscript{23} Also, new tests have been developed for detecting liver fibrosis, such as ultrasound devices and procollagen III tests, although more studies are clearly needed to identify the value and cost/benefit of these new methods for the early diagnosis of liver fibrosis.

Cyclosporine (CYA) is another effective agent in the management of psoriasis, and, as with MTX, there are major concerns regarding its safety. It is key to assess at baseline and then to monitor renal function, blood pressure, serum chemistry including K\textsuperscript{+} and Mg\textsuperscript{++}, lipid panel, and CBC. Among the most common AEs associated with the use of CYA are nephrotoxicity, hypertension, hypomagnesemia, hyperkalemia, hyperlipidemia, drug interactions, hypertrichosis and lymphoproliferative disease.\textsuperscript{24}

In a double-blind, placebo-controlled, multicenter, crossover study, amlodipine significantly reduced serum creatinine compared with placebo in patients receiving CYA.\textsuperscript{25} It is relevant to note that calcium channel blockers such as amlodipine are also indicated to treat CYA-associated hypertension. Hyperkalemia associated with CYA is usually treated with hydrochlorothiazide; magnesium depletion is managed by magnesium supplements, while dyslipidemia can be addressed with pravastatin. Hyperlipidemia is a common side effect of oral retinoid treatment.

Management of acitretin-induced hyperlipidemia was assessed in a double-blind crossover study.\textsuperscript{26} Triglycerides and cholesterol were significantly reduced in 22 patients treated with gemfibrozil (p<0.01 and p<0.05 respectively) compared with placebo after 8 weeks of therapy. There were no negative effects of gemfibrozil on acitretin dose response nor clinical side effects.

Cumulative toxicity is a well-known side effect of several psoriasis therapies. The increased incidence of squamous cell carcinomas following long-term PUVA treatment is well established. Acitretin has been shown to reduce the incidence of squamous cell carcinoma (SCC) in transplant patients.\textsuperscript{27} A randomized, double-blind, placebo-controlled trial in 44 renal transplant patients reported that the incidence of SCC was 11\% in the acitretin group, compared with 47\% in the placebo group (p<0.01). There was also a significant decrease in the number of keratotic lesions in the group treated with acitretin. It also decreases the incidence of new squamous cell carcinomas in patients with long-term PUVA treatment history.\textsuperscript{28}

Effective treatment and sustained remission are sometimes difficult to achieve. In these situations, combination therapy may be the best treatment option. Topical therapies are often combined with systemic agents...There is wide-ranging experience in combining systemic agents to treat psoriasis.
Apremilast is an oral phosphodiesterase-4 (PDE-4) inhibitor. A randomized, controlled, phase 3 trial (ESTEEM 1) assessed the safety and efficacy of apremilast in moderate to severe psoriasis. Patients were assigned to receive placebo (n=282) or apremilast 30 mg twice daily (n=560) for 16 weeks. Patients experienced significant clinical improvement at week 16: 33.1% of patients treated with apremilast achieved PASI 75 versus 5.3% for the placebo group. Similarly, 58% achieved PASI 50 versus 17% for those on placebo (P < 0.0001). There were also statistically significant differences for the static Physician’s Global Assessment (sPGA 0–1) (21.7% vs. 3.9%, respectively; P < 0.0001).

PASI 75 benefits were greater in patients who had received no previous systemic or biologic therapy (38.7% and 35.8%, respectively); about 27% of those who had not responded to TNF inhibitors achieved a PASI 75 response. Intestinal intolerability is a well-known adverse effect with PDE4 inhibitors. The events reported for apremilast included diarrhea and nausea (18.8% and 15.7% for apremilast versus 7.1% and 6.7% for placebo). Gastrointestinal (GI) adverse effects were most common within the first 15 days of the first dose, and most events resolved within an additional 15 days. Fewer than 2% of patients withdrew due to these adverse effects. Severe adverse events were reported in 3.6% of apremilast patients and in 3.2% of placebo patients. No cases of tuberculosis or lymphoma and no increases in cardiovascular risk or opportunistic infections were reported.

Recently, the FDA approved apremilast for treating psoriatic arthritis. A 24-week, phase 3, randomized placebo-controlled trial (PALACE 1) assessed the long-term efficacy of apremilast for treating psoriatic arthritis in 504 patients. At week 16, there was significant improvement in the modified American College of Rheumatology response criteria (ACR20) in patients treated with apremilast compared to placebo. ACR20 was achieved in 31% and 40% of the patients receiving 20 mg twice a day (BID) or 30 mg BID respectively, compared to 19% for the placebo group (p<0.001).

There were also significant improvements in physical function and psoriasis measures in both apremilast groups compared to placebo, although 30-mg, twice-daily doses generally had higher response rates. As in other studies, the most common adverse events were gastrointestinal and generally occurred early, were self-limiting, and rarely led to discontinuation. No significant differences were observed in major adverse cardiac events, serious or opportunistic infections, malignancies or laboratory abnormalities. Apremilast has shown an acceptable safety profile and was generally well tolerated.

Tofacitinib is an oral Janus kinase (JAK) inhibitor under investigation as a potential treatment for plaque psoriasis and psoriatic arthritis. In a phase 2b, 12-week study, 197 patients were randomized to tofacitinib 2, 5, or 15 mg, or twice-daily placebo. PASI score, body surface area and target plaque severity score (TPSS) were measured. At week 12, mean improvements in PASI and body surface area values were significantly greater with tofacitinib doses compared to placebo. In responsive as well as in typically nonresponsive areas, there was a statistically significant improvement.
improvement in TPSS with tofacitinib 2, 5, and 15 mg twice daily compared to placebo.

A different analysis of the same trial showed that at week 12, PASI 75 response rates were significantly higher for all tofacitinib groups: 25% (2 mg, p <0.001), 40.8% (5 mg, p < 0.0001) and 66.7% (15 mg, p<0.0001), compared with placebo (2.0%). Among the most common AEs, dose-dependent increases from baseline in mean serum high-density lipoprotein, low-density lipoprotein and total cholesterol, and decreases in hemoglobin and neutrophils were observed. These results show that short-term treatment

The AAD meeting included a discussion of five new biologics under study as psoriasis treatments: certolizumab, secukinumab, ixekizumab, brodalumab, and tildrakizumab. Certolizumab is also being evaluated as a treatment for psoriatic arthritis.

with oral tofacitinib achieves clinical improvement in patients with moderate to severe plaque psoriasis.

**Biologics**

Drs. Gottlieb and Lebwohl led a discussion of new biologics.

Certolizumab (CZP) is a PEGylated Fab’ fragment of a humanized TNF inhibitor monoclonal antibody. A randomized, placebo-controlled, double-blind study evaluated the efficacy and safety of certolizumab in 176 patients with moderate to severe psoriasis. Patients were treated with 200 mg, 400 mg or placebo every other week. At 12 weeks, PASI 75 was achieved by 75%, 83% and 7% of patients in the 200 mg, 400 mg and placebo groups, respectively (P<0.001 for both treatment groups versus placebo).

A re-treatment extension study was performed with 71 PASI 75 responders who relapsed within a 12 to 24-week period without treatment. Median PASI scores were similar at week 12 in both the first treatment and re-treatment periods. Serious adverse events occurred in 3%, 5% and 2% of the 200 mg, 400 mg and placebo patients, respectively.

An ongoing phase 3 trial of patients with psoriatic arthritis (PsA) evaluated the efficacy and safety of CZP after 24 weeks. A total of 409 patients received placebo, 200 mg every 2 weeks or 400 mg every 4 weeks. At week 12, ACR20 response was significantly greater in the 200 mg and 400 mg patients than placebo (58.0% and 51.9% versus 24.3% [p<0.001]). There were also sustained improvements in psoriatic skin, enthesitis, dactylitis and nail disease. ACR20 response with CZP was independent of prior TNF inhibitor exposure. No changes in the safety profile of certolizumab were found. The authors concluded that certolizumab showed rapid improvements in the signs and symptoms of PsA, including joints, skin, enthesitis, dactylitis and nail disease.

Secukinumab is a monoclonal antibody directed against IL-17A. A randomized, placebo-controlled clinical trial assessed the efficacy and safety of secukinumab in moderate to severe psoriasis. At 12 weeks of treatment, secukinumab 3×150 mg and 3×75 mg at weeks 0, 4 and 8 resulted in significantly higher PASI 75 response rates vs. placebo (82% and 57% versus 9%; P< 0.001 and P=0.002, respectively). At week 12, the PASI 90 response was significantly higher in the 3×150 mg group vs. placebo (52% vs. 5%). Secukinumab was well tolerated. Two cases of neutropenia were reported in the 3×150 mg cohort. Other studies with secukinumab have shown similar high efficacy. The ERASURE study showed that secukinumab rapidly improved plaque psoriasis, and sustained high efficacy up to 52 weeks. At week 12, rates of PASI 75 responses were 72% in the secukinumab 150-mg group and 82% in the 300-mg group. PASI 90 response rates were 39% and 59% among the 150-mg and 300-mg secukinumab groups, respectively, and 1% in the placebo group (P< 0.01). No new or unexpected safety findings were observed with secukinumab.

Ixekizumab, a humanized anti-interleukin-17 monoclonal antibody, has been tested as a psoriasis treatment. In a phase 2, double-blind, placebo-controlled trial, 142 patients with chronic moderate to severe plaque psoriasis
received 10, 25, 75, or 150 mg of ixekizumab or placebo at 0, 2, 4, 8, 12, and 16 weeks. At 12 weeks, the percentage of patients achieving PASI 75 was significantly higher with ixekizumab (except with the lowest, 10-mg dose) at 82.1% (150 mg), 82.8% (75 mg), and 76.7% (25 mg), compared with placebo (7.7%, \( P < 0.001 \)). The percentage of patients achieving PASI 90 for each group was 71.4% (150 mg), 58.6% (75 mg), and 50.0% (25 mg) versus placebo (0%, \( P < 0.001 \)). Similarly, a PASI 100 was achieved in significantly more patients in the 150-mg group (39.3%) and the 75-mg group (37.9%) than in the placebo group (0%) (\( P < 0.001 \)). The onset of clinical differences was as early as 1 week and was sustained through 20 weeks. Adverse events were present similarly in both groups. No serious adverse events or major cardiovascular events were observed.

Brodalumab is a human anti-interleukin-17-receptor monoclonal antibody. A randomized, placebo-controlled clinical trial evaluated the efficacy of brodalumab to treat moderate to severe psoriasis.\(^{38}\) A total of 198 patients received brodalumab (70 mg, 140 mg, or 210 mg at day 1 and weeks 1, 2, 4, 6, 8, and 10 or 280 mg monthly) or placebo. At week 12, PASI 75 and 90 responses were seen in 77% and 72%, respectively, of the patients in the 140-mg brodalumab group and in 82% and 75%, respectively, of the patients in the 210-mg group, as compared with 0% in the placebo group (\( P < 0.001 \) for all comparisons). Two cases of grade 3 neutropenia were reported in the 210-mg brodalumab group. Other studies such as OLE II have also shown similar results in efficacy and safety with brodalumab.

IL-17 and IL-23 play a fundamental role in skin host defense against candida albicans; furthermore, inborn errors of human IL-17 immunity are related with the development of mucocutaneous candidiasis. It is important to note that long-term studies and more patient years of exposure are needed to determine more accurately the safety of these new agents.

Tildrakizumab is an anti-IL-23p19 monoclonal antibody. A phase 2b randomized, placebo-controlled trial to assess efficacy in psoriasis showed significant clinical improvement at 16 weeks. PASI 75 was achieved by 76.2%, 67.1%, 65.5%, 35%, and 4.9% in the 200-mg, 100-mg, 25-mg 5-mg and placebo groups, respectively. PASI 90 was achieved by 51.2%, 38.2%, 24.4%, 11.9% and 2.2% in the 200-mg, 100-mg, 25-mg, 5-mg, and placebo groups, respectively (\( P \leq 0.001 \)). There was no dose-dependent increase in adverse events across treatment groups. Within the first 16 weeks of treatment, 4 serious adverse events were reported: bacterial arthritis (possibly related) with tildrakizumab 25 mg; death (unlikely related) with 100 mg; ovarian cyst (unlikely related) with 200 mg; and lymphodema (possibly related) with 200 mg. Further studies are required to clearly establish the safety profile for this agent.

As many biologic patent restrictions are coming to an end, biosimilars were also addressed. The experience of India was presented, particularly the case of rituximab and the introduction of a generic form of rituximab in 2007. The market price was one-third of the original medication and after its introduction, the number of treated patients increased sixfold. Efficacy and safety of the biosimilars is an ongoing subject of concern and will probably have to be addressed in a case-by-case basis.

Clinical presentations
IPC Councilor Dr. Andrew Blauvelt of the Oregon Medical Research Center, Portland, discussed clinical presentations and off-label use of biologics. Although psoriasis is a clinically heterogeneous disease, clinical trials are usually performed with the most common clinical variant, plaque psoriasis. There are several forms of psoriasis for which few or no randomized controlled clinical studies have been conducted. These less common clinical presentations

There are several forms of psoriasis for which few or no randomized controlled clinical studies have been conducted, including erythrodermic, palmoplantar and pustular psoriasis. However some case reports show the use of ustekinumab as an effective therapeutic option for these conditions.
include erythrodermic, palmoplantar and pustular psoriasis among others. However Dr. Blauvelt presented some case reports that show ustekinumab as a therapeutic option for these conditions:

- For erythrodermic psoriasis, several case reports have shown that ustekinumab can be used effectively in the treatment of erythrodermic and sub-erythrodermic psoriasis that is unresponsive to TNF-α inhibitors.

- Palmoplantar psoriasis: In an investigator-initiated, open-label clinical trial for the treatment of palmoplantar psoriasis, 20 patients received standard doses of ustekinumab. After 16 weeks of treatment, 35% of subjects achieved clinical clearance; 67% of those receiving a 90-mg ustekinumab dose achieved clinical clearance compared with 9% receiving 45-mg (p=0.02).

- Palmoplantar pustular psoriasis (PPP): A 2011 case report presented 2 cases of refractory PPP that were treated off label effectively with ustekinumab. It is important to consider that other reports and personal experience have shown different outcomes in this particular variant of psoriasis treated with ustekinumab.

- TNF-α antagonist-associated psoriasis: Induction and exacerbation of psoriasis have been linked to treatment with TNF-α inhibitors. Although this association is unusual, a case report has shown that ustekinumab can be used effectively as a treatment for this rare complication.

Special groups

Pediatric psoriasis
Dr. Kelly M. Cordoro of the dermatology department, University of California, San Francisco, discussed pediatric psoriasis.

In 2013, researchers conducted a national, multi-center, cross-sectional study of 181 children ages 5 to 17 to determine the prevalence of scalp and nail involvement and a history of guttate psoriasis. Of the 181 participants, 143 (79.0%) reported a history of scalp involvement and 71 (39.2%) described a history of nail involvement. Scalp and nail involvement were not related to psoriasis severity. Children with severe psoriasis (35.9%) more often reported a history of guttate lesions than did those with moderate psoriasis (21.8%) (p=.02). History of streptococcal infection was more common in children with guttate than those with plaque psoriasis at onset (p=.02) but did not correlate with severity. Based on these results, the study concluded, more aggressive monitoring and management should be considered for guttate psoriasis, considering its association with more severe disease.

A multicenter, cross-sectional study of 409 psoriatic children was conducted to assess the relationship of excess and central adiposity with pediatric psoriasis severity. Excess adiposity (body mass index ≥85th percentile) was found in 37.9% of children with psoriasis versus 20.5% of controls but did not differ significantly by severity. The odds ratio (95% CI) of presenting obesity (body mass index ≥95th percentile) overall in children with psoriasis versus controls was 4.29 (1.96-9.39). Waist-to-height ratio was significantly higher in the psoriatic group (0.48) versus the control group (0.46) but was unaffected by psoriasis severity. Children who had a history of severe psoriasis but whose condition was mild when they enrolled, showed no significant difference in adiposity from children whose psoriasis was severe when they enrolled and remained severe. Overall, regardless of psoriasis severity, children with psoriasis tend to have excess adiposity and increased central adiposity.

Pregnancy in psoriasis
Dr. Jenny Murase of the Palo Alto Foundation Medical Group, University of California, San Francisco, presented data on psoriasis and pregnancy.

Management of psoriasis in pregnant women can be challenging, as several of the medications commonly used are teratogenic or abortifacient. Although topical-steroid exposure during pregnancy was not associated with orofacial cleft, low birth weight, preterm delivery, fetal death or low Apgar score, it was associated with increased...
risk of low birth weight when the amount dispensed of potent/very potent exceeded 300 g.  

Phototherapy in pregnant women is considered safe when narrowband UVB is used. PUVA therapy can decrease folic acid levels; there are no reports of PUVA or UVB light therapy increasing neural tube defects. Oxsoralen is a mutagen and, therefore, should not be used in pregnant women. Cyclosporine is categorized as class C in the FDA’s drug formulary. No increase in malformations was reported, although there is concern regarding possible growth restriction associated with its use.

Data on the use of biologics during pregnancy are still controversial. The use of TNF inhibitors could be associated with an increased risk of spontaneous abortions. It is a common practice to stop biologics during pregnancy, as up to 60% of psoriasis patients will improve spontaneously. There are pregnancy registries that encourage enrolling patients if pregnancy occurs while on a biologic or within 8 weeks of treatment. The following phone numbers correspond to the registries mentioned: adalimumab 877-311-8972; cyclosporine 888-522-5581; etanercept 877-311-8972; and infliximab 800-457-6399.

Comorbidities

IPC Councilor Dr. Jashin J. Wu of Kaiser Permanente, Los Angeles Medical Center, discussed comorbidities in psoriasis.

Evidence associating psoriasis with increased risk of cardiovascular disease is growing. Studies by dermatologist Joel Gelfand of the Hospital of the University of Pennsylvania, Philadelphia, and cardiologist Nehal Mehta of the National Heart, Lung and Blood Institute have shown that TNF-α antagonists can decrease the risk of myocardial infarction (MI) in patients with psoriasis. Even so, Dr. Wu did not recommend prescribing TNF inhibitors specifically to reduce the risk of MI, as there is not enough evidence to recommend therapies for psoriasis based solely on cardiovascular impact.

For monitoring purposes, the National Psoriasis Foundation recommends measuring blood pressure, pulse, and body mass index every 2 years; fasting blood glucose and lipid levels every 5 years or every 2 years if patient has additional risk factors; and assessment of joint status at every visit.  

References

A REPORT FROM THE AMERICAN ACADEMY OF DERMATOLOGY
72ND ANNUAL MEETING


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A REPORT FROM THE 2014 RADLA MEETING IN SANTIAGO, CHILE

Highlights from the XXXII Reunión Anual de Dermatólogos Latinamericanos (RADLA) - the Annual Meeting of Latin American Dermatologists

A conversation with Dr. Claudia de la Cruz

Dr. Claudia de la Cruz is director of Clínica Dermacross, Santiago de Chile. An educator and practitioner with longtime expertise in psoriasis, she was a member of the 2014 RADLA scientific committee.

What is RADLA?

The Reunión Anual de Dermatólogos Latinamericanos (RADLA), or Annual Meeting of Latin American Dermatologists, takes place each year in Latin America, with representatives coming from each country in this region. This year marked the 32nd annual meeting, with 2,500 dermatologists from 30 countries and 1,400 industry representatives attending. RADLA provides an opportunity for various dermatological societies to share knowledge and information.

Education was a primary goal of RADLA’s founders. They felt it was important for resident physicians to learn from experts from other countries as well as their own in order to understand the different approaches to problems.

As a result, many young people attend this congress, which includes a special area for young dermatologists to present their research. Prizes are awarded to students and residents who present their research here.

What role did psoriasis play in this annual meeting?

For many years, psoriasis has been generally undertreated. It was thought to be an aesthetic disease. Plaques were seen as something that could be hidden and not affect the overall health of the patient. In the past 15 years, there has been a real change in how doctors, educators and researchers understand and treat psoriasis. At this year’s conference, psoriasis was featured in at least one session per day. This indicates that there is much greater focus on this disease in dermatology now. This also helped the attendees understand that perception of this disease has drastically changed, and we now know that psoriasis is a systemic disease.

What is RADLA’s role in pushing forward the way dermatologists think about psoriasis?

Latin America has a large population with a distinct genetic makeup. It is important that we understand this genetic component to be able to better treat psoriasis. At RADLA, dermatologists from across Latin America were able to discuss this aspect of the disease and share their individual experiences. More remains to be done. For example, we presume that the prevalence of psoriasis in Latin America is similar to that of the rest of the world, but we do not really know. At RADLA, we have an opportunity to focus on these regional issues and determine how to confront them together.

This year’s meeting took place in Santiago, Chile. As the head of the Chilean Psoriasis Group SOCHIDERM, how do you think it influenced psoriasis research, education and treatment in your country?

We need more Latin American dermatologists to be involved in psoriasis research and publishing. During RADLA, dermatologists were able to learn about recent psoriasis research and the many new small molecules under investigation for psoriasis treatment. We hope this meeting in Chile has encouraged more involvement in treating patients who have psoriasis.

What are some highlights from the psoriasis sessions presented at RADLA?

The discovery of many new molecules in psoriasis research was extensively discussed. We now have a much bigger treatment arsenal available, especially for patients with moderate to severe psoriasis. For instance, in a session discussing the biologic secukinumab, Dr. Richard Langley shared research that is making great advances. In the past, we hoped for Psoriasis Area Severity Index (PASI) 75...
A REPORT FROM THE 2014 RADLA MEETING IN SANTIAGO, CHILE

responses. Now we look for even higher responses, and we want patients to have even clearer skin. It is interesting to see how this promising drug clears the skin quickly and with few adverse events. We hope it will launch next year.

It is encouraging to see the results of other new treatments in development, such as tofacitinib and ixekizumab. I hope that these new options and the information presented at this conference will encourage Latin American dermatologists to prescribe more systemic treatments for this disease because most of our patients are now undertreated. Many are still receiving topical treatments even if they have a severe form of the disease.

Please elaborate on the issue of access to more advanced therapies.

In most of Latin America, patients with psoriasis have access to nearly all of the available treatments. In Chile, the public health system offers only methotrexate for moderate to severe psoriasis. Some public hospitals offer phototherapy. But patients have no access to biological therapies. The Chilean Psoriasis Group is working with the national ministry of health and the Psoriatic Patients Group to make all treatment options available. We look forward to having approval later this year.

This is the fourth RADLA meeting attended by the International Psoriasis Council. Why is it important for IPC to participate?

RADLA is the major Latin American conference, and the dermatological community here is getting more familiar with the work of IPC through its participation. Being part of this conference is essential for becoming well known and able to work in this region.

What were some of the highlights of the IPC Meet the Experts Program that you co-chaired with IPC founding President Alan Menter?

Dr. Menter shared a psoriasis case study with us on psoriasis and Hodgkins disease. It was valuable for us to learn from him as he presented his challenging case and also in discussing our own cases and the work that we do.

Additionally, IPC’s Meet the Experts program allowed us to share cases from different Latin American countries and discuss treatment methods based on access to certain therapies in other nations. It is important to have IPC members from Latin America in order to share our thoughts with one another and to include the experience of our region as part of the worldwide discussion on psoriasis.

Chilean researcher presents at AAD

At the American Academy of Dermatology (AAD) annual meeting last March, Chilean dermatologist Fernando Valenzuela presented the results of a study he and his associates conducted titled, “Comparison of tofacitinib versus etanercept or placebo in moderate-to-severe chronic plaque psoriasis: a phase 3 randomized trial.”

It was a proud moment for Chile’s dermatology researchers, who are involved in several research projects studying new drugs in dermatology, such as tofacitinib, noted IPC Councilor Dr. Claudia de la Cruz. “It is unusual that a Chilean dermatologist shares the results of his research at major conferences, such as the AAD meeting. We could not be more pleased that Dr. Valenzuela represented our country as a top researcher at such an important meeting.”

De la Cruz is hoping that Valenzuela’s presentation at AAD will encourage more Chilean researchers to become involved in psoriasis research.
IPC NEWS

IPC’s LEADERSHIP

January of 2014 brought several important changes in IPC’s leadership. In addition to welcoming a new board president, Chris Griffiths, IPC also brought on a new CEO, Steve O’Dell, who is profiled here. A conversation with Griffiths begins on page 24.

Steve O’Dell takes the helm at IPC

Steve O’Dell, whose background includes more than 24 years as a leader in both for-profit and nonprofit health care companies, joined IPC in January as its new chief executive officer.

As head of IPC, O’Dell is charged with expanding the organization’s programming and increasing financial support for its research and education efforts. He will also work to enhance IPC’s influence in the dermatology field through partnerships with scientific organizations, representatives from industry and academia, health care vendors, and other public and private organizations.

“This project, and many more to be announced, will address key issues and needs of all stakeholders. It will also solidify IPC as the pre-eminent voice and the preferred professional organization with which to collaborate to provide leadership and guidance regarding the full spectrum of psoriasis in research, education and improvement of patient care worldwide.”

Before joining IPC, O’Dell had been the owner and president of a home health care and medical staffing business which he began in 2008. Before that, he held several leadership positions within the biopharmaceutical industry for companies that included Genentech, Centocor (now Janssen Biotech Inc.), and Parke-Davis Pharmaceuticals. His expertise includes in-depth knowledge of psoriasis and immunology.

O’Dell’s extensive background as a volunteer includes serving as board member, adviser and member for numerous nonprofit organizations, among them the Alzheimer’s Association, United Way, March of Dimes, and the American Heart Association.

“Steve’s wealth of experience as a senior-level executive in the health care field makes him the ideal leader to build on IPC’s successful 10-year history, and guide the organization to the next level,” says IPC board president Professor Christopher Griffiths. “He has the right combination of expertise, familiarity with industry, and management skills to advance IPC’s vision to improve scientific knowledge and bring the best care to all patients coping with psoriasis and its attendant comorbidities.”

As an example, O’Dell cited IPC’s recently-announced partnership with the International Federation of Psoriasis Associations (IFPA) and the International League of Dermatological Societies (ILDS) to develop a Global Psoriasis Atlas, a database of information on the prevalence of psoriasis worldwide and by country. Its long-term goal, O’Dell said, is to improve understanding of psoriasis and how it affects the individual and society.
Please join us at a reception during EADV to honor IPC’s 10-Year Anniversary!

Friday, October 10, 2014
6:30 - 8:00 p.m.

For more information and location, email events@psoriasiscouncil.org

Meet IPC’s new board president, Chris Griffiths, IPC’s new CEO, Steve O’Dell, and IPC’s Councilors and friends from around the world.

Help us celebrate how far we’ve come and raise our glasses to many successful years ahead!
Moving forward: Q&A with IPC Board President
Professor Christopher Griffiths, MD

In January, Professor Chris Griffiths, a co-founder of the International Psoriasis Council, became the organization’s new board president. He replaced Professor Peter van de Kerkhof, MD, PhD, who stepped down as president after a three-year tenure.

Griffiths, who has devoted his career to psoriasis research, education and clinical care, is Foundation Professor of Dermatology at the University of Manchester, United Kingdom. He received his medical training from St Thomas’ Hospital Medical School, London University, and trained in dermatology at St Mary’s Hospital, London, and at the University of Michigan.

He helped develop the “hub-and-spoke” model of dermatology services for Greater Manchester, and, with his colleague Dr. Robert Chalmers, introduced the Manchester Psoriasis Service, a multidisciplinary clinic for severe psoriasis that was awarded Hospital Doctor Dermatology Team of the Year in 2002. In 2011, he was elected to Fellowship of the Academy of Medical Sciences and was appointed as a National Institute for Health Research senior investigator.

This year, he led a successful bid to the Medical Research Council to establish a coalition of dermatologists, scientists, industry partners and psoriasis patients, the Psoriasis Stratification to Optimize Relevant Therapy (PSORT) stratified medicine consortium. The consortium will investigate how to use clinical, genetic and immune biomarkers to determine personalized treatment plans for patients with psoriasis.

Griffiths has served as president of the British Association of Dermatologists, the European Dermatology Forum, and the British Society for Investigative Dermatology. He is an executive board member of the International League of Dermatological Societies and is the senior editor of Rook’s Textbook of Dermatology.

He lives in Hale, South Manchester, with his wife, Tamara, also a dermatologist. They have two daughters, Caitlin, who has just started her medical school studies at University College, London, and Georgina, who is still in school.

In an interview Griffiths talked about IPC, his role as its new board president and how he relaxes when he manages to find some free time.

You helped establish IPC in 2004 and have been a leader in the organization ever since. What motivates you to give your time and expertise to this organization?

I care passionately about improving the lives of people with psoriasis and am convinced that this can only be achieved by clearly understanding the causes of the disease and using this knowledge to educate healthcare practitioners.

Why psoriasis in particular?

Psoriasis interests me because it affects a large number of people and is the first disease I started researching when I was a dermatology registrar in London. One of the people (a GP) who influenced me to study medicine suffered from psoriasis. That may have been a subliminal reason, also.

What do you see as IPC’s purpose and what is your role as its board president?

IPC’s role is to effect collaboration among leaders in psoriasis research, education and clinical management to further our understanding of the disease and minimize its impact on the individual and on society. I am privileged to have been elected to lead IPC and hope to be able to advance these goals over the next three years.

What are the main challenges facing IPC?

Perhaps the main challenge is to establish our brand identity, that is, what is our business? The other challenges are to maintain our funding stream, to decrease our reliance on industry funding and to elevate our influence globally.

What is your vision for IPC? What would you like to accomplish?

Overall, I would wish for recognition that IPC is the leading organization for those interested in research, education and management of psoriasis and its comorbidities. In the first year, we should move our groundbreaking scientific
IPC NEWS

program forward by completing stage one of our project to complete a genetic map of psoriasis, initiating the Global Psoriasis Atlas Project, and increasing the reach of our popular Meet the Experts sessions.

Do you have a message for IPC councilors?

I am immensely honored to lead the IPC. The success of this organization is only possible through the dedication of its councilors and board members, who give their time freely to our goals of advancing knowledge and enhancing care of patients with psoriasis.

What are your hobbies & interests? What’s your favorite thing to do when you have spare time?

My downtime (such as it is) is spent exploring the beautiful countryside of the Mawddach estuary in West Wales, long distance running, cycling, and gardening. I travel so much as part of my academic life that being either at home or in Wales is the best way for me to unwind.

TREATMENT

Biosimilars symposium: A first for IPC!

With the goal of educating dermatologists about issues related to biosimilar drugs, IPC will sponsor a first-in-a-series symposium on the topic Saturday, Oct. 11, 5-6:30 pm, during the annual meeting of the European Academy of Dermatology and Venereology (EADV) in Amsterdam.

“The IPC 2014 Crossfire Symposium: The Advent of Biosimilars” will feature experts ranging from academic and industrial representatives to innovators and regulators who will discuss the most important and controversial elements associated with biosimilars, also known as “follow-on biologics.”

Among its objectives, the symposium will discuss biosimilars’ clinical use in dermatology; highlight biologics’ global potential; address regulatory, safety and immunogenicity issues; and review European and U.S. Food and Drug Administration approvals of biosimilars to date.

IPC plans to offer biosimilars-related symposia at international meetings in 2015 and beyond.

The symposium expands IPC’s current biosimilars program, which includes a 12-member task force. The group met at the 76th Annual Meeting of the American Academy of Dermatology in Denver in March. Members agreed to draft a position paper that provides practical information to dermatologists on how biosimilars might affect their practices.

Andy Blauvelt (United States) led the task force discussion. Attending the meeting were Ricardo Romiti (Brazil), Lluis Puig (Spain), Lone Skov (Denmark), Claus Zachariae (Denmark), Murlidar Rajagopalan (India), Jashin Wu (United States), and Sergio Chimenti (Italy). Errol Prens (Netherlands) and Helen Young (UK) participated by phone.

Topical Therapy Working Group

IPC’s Topical Therapy Working Group also met at the AAD annual meeting. The group decided to create a global inventory of topical therapy guidelines and investigate the current gaps in knowledge related to topical therapies. Lars Iversen (Denmark) led the meeting. Attending were IPC Councilors Charles Lynde (Canada), André Vicente Esteves de Carvalho (Brazil), and Linda Stein Gold (United States). Councilors Brian Kirby (Ireland), Elise Kleyn (United Kingdom), and Peter van de Kerkhof (Netherlands) participated by phone.

EDUCATION

IPC offers new CME series

IPC has launched a new CME (continuing medical education) series of dinner meetings designed to educate healthcare providers about the latest information on comorbidities and new options for treatment. The series, titled “The Shifting Paradigm in Psoriasis Treatment,” aims to reach dermatologists, physician assistants, nurse practitioners and other healthcare providers involved in the care of patients with psoriasis. Meetings have already taken place in Dallas, Boston, New York City and St. Louis.

More information about the series is available at www.psoriasiscouncil.org. Click on “Education” on the left side of the page. You can watch a video of the New York City meeting at www.psoriasiscme.tv.
RESEARCH PARTNERSHIP

Global Atlas project launches
With a long-term goal of documenting the global prevalence and burden of psoriasis, IPC has joined with two other worldwide organizations – the International Federation of Psoriasis Associations (IFPA) and the International League of Dermatological Societies (ILDS) – to form the Global Psoriasis Atlas project. This project will collect data from as many countries as possible to increase understanding of the global burden of the disease and also its economic impact. “The data collected by this project will be used to advocate for improved treatment, access to care and recognition of psoriasis as a priority,” said IPFA President Lars Ettarp. You can find a full press release about the Atlas project at www.psoriasiscouncil.org/news.htm.

IPC COUNCILORS

New councilors appointed
Since January, the IPC Board of Directors has appointed four additional councilors. IPC Councilors serve in an advisory capacity and lend their global expertise on psoriasis research, treatment, and education to support all IPC programs, events, and initiatives. They provide expert opinion on current psoriasis therapeutic and research-related issues, participate in roundtable conferences as well as contribute manuscripts to top-tier journals and make presentations before congresses around the world. The new councilors are:

April Armstrong, MD
Denver, Colorado
Dr. Armstrong is vice chair of clinical research, associate professor of dermatology, director of clinical trials and outcomes research, and director of the dermatology department’s psoriasis program at the University of Colorado Denver. She has a medical degree from Harvard Medical School and a master’s in public health from Harvard School of Public Health. Before joining CU Denver, Dr. Armstrong was director of the psoriasis clinic’s Teledermatology Unit at the University of California Davis. She has authored more than 130 scientific papers and served as an editor of Principles of Pharmacology. Dr. Armstrong holds leadership posts in several professional groups, including the American Telemedicine Association, National Psoriasis Foundation medical board, and the American Academy of Dermatology. She is on the editorial boards of JAMA Dermatology, Journal of the American Academy of Dermatology, and Telemedicine and eHealth.

Claudia de la Cruz, MD
Santiago, Chile
Dr. de la Cruz is the director of Clínica Dermacross in Santiago de Chile. She obtained her medical and dermatology degree from Universidad de Chile. She is a former assistant professor at the Universidad Católica de Chile, former director and current member of the Chilean Society of Dermatology. Dr. de la Cruz also is the coordinator of the Chilean Psoriasis Group, a member of the National Ministry of Health Committee for Psoriasis Disease, and a member of GRAPPA (Group for Research and Assessment of Psoriasis and Psoriatic Arthritis). She is active in educational programs related to psoriasis for dermatologists, author of papers in Latin America, and a researcher for various pharmaceutical companies.

Johann Gudjonsson, MD, PhD
University of Michigan, Ann Arbor
Dr. Gudjonsson graduated from the University of Iceland Medical School and completed his internship and dermatology residency training at the University of Michigan. In 2008, Dr. Gudjonsson joined the faculty of the university’s dermatology department. Dr. Gudjonsson sees general dermatology patients at the University of Michigan Taubman Center and directs the inpatient consultation service. Building on investigative dermatology training completed in Iceland, Dr. Gudjonsson has been performing basic immunological and genetic work on psoriasis at the university. His primary research focus is basic immunological and genetic research on psoriasis. He received the American Academy of Dermatology’s Young Investigator Award in 2007 and his work has earned several...
research awards, including awards from the American Skin Association and the Dermatology Foundation.

Nehal Mehta, MD
Bethesda, Maryland
Dr. Mehta attended an accelerated 7-year biomedical program, receiving his medical degree in 2001 from George Washington University. He earned a master of science degree in clinical epidemiology (MSCE) with a concentration in human genetics from the University of Pennsylvania in 2009, and completed his chief medical residency in internal medicine at the University of Pennsylvania Hospital. In 2009, Dr. Mehta joined the university’s School of Medicine faculty. In 2012, he became the National Institute of Health’s inaugural Lasker Clinical Research Scholar and joined the NHLBI’s cardiovascular and pulmonary branch. Dr. Mehta has received numerous local and national awards and is active in several organizations, including the American Heart Association and National Psoriasis Foundation. He edits the section on cardiovascular, metabolic, and lipoprotein translation in the Journal of Translational Medicine and is an associate editor for BMC Cardiovascular Diseases and the American Journal of Cardiovascular Diseases.

IN OTHER NEWS

Psoriasis goes global
IPC applauds the resolution adopted by the World Health Assembly in May that will greatly increase global awareness of psoriasis and its often devastating effects. The assembly, an arm of the World Health Organization, recommends that WHO member states find ways to educate the public about the disease and asks the WHO Secretariat to publish a global report on psoriasis, emphasizing research and outlining ways for member states to include psoriasis in any plans aimed at treating and reducing noncommunicable diseases. Read more about it at www.psoriasiscouncil.org/who_resolution.htm.

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RESOURCES

The International Psoriasis Council is pleased to bring you the following educational opportunities to advance your knowledge of treating patients with psoriasis.

UPCOMING IPC EVENTS

- **August 15, 2014**
  - **IPC Meet the Experts**
  - Vancouver, Canada
  - 68th Meeting of the Pacific Dermatologic Association

- **September 10, 2014**
  - **IPC Symposium on Developing a Global Psoriasis Atlas: Setting the Standard for Evidence on the Global Epidemiology of Psoriasis**
  - Copenhagen, Denmark
  - 44th European Society for Dermatological Research Meeting

- **September 27, 2014**
  - **IPC Meet the Experts**
  - Montevideo, Uruguay
  - 14th Uruguayan Congress of Dermatology

- **October 10, 2014**
  - **IPC Meet the Experts**
  - Amsterdam, Netherlands
  - 23rd Congress of the European Academy of Dermatology & Venereology

- **October 11, 2014**
  - **IPC’s Crossfire Symposium: The Advent of Biosimilars**
  - Amsterdam, Netherlands
  - 23rd Congress of the European Academy of Dermatology and Venereology

- **December 4, 2014**
  - **IPC Meet the Experts**
  - Cancun, Mexico
  - 2° Congreso Latinoamericano de Psoriasis

- **December 11 – 13, 2014**
  - **Psoriasis: From Gene to Clinic 7th International Congress**
  - London, England

- **June 8 – 13, 2015**
  - **23rd World Congress of Dermatology**
  - Vancouver, Canada

- **July 8 – 12, 2015**
  - **4th World Psoriasis & Psoriatic Arthritis Conference**
  - Stockholm, Sweden

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